REMARKS

Status of Claims

Claims 1-3 and 7-8 were pending. Upon entry of this Amendment, Claims 1-3 and 7-27 will be pending. Claim 1 is currently amended, and Claims 9-27 are newly added. Support for this claim amendment and for the newly introduced claims is found throughout the specification as filed. Accordingly, no new matter is introduced by way of these amendments.

Claim Rejections

Claim Rejections Under 35 U.S.C. §112, Written Description

The Examiner maintained the rejection of Claims 1-3 and 7-8 as allegedly failing to comply with the written description requirement. The Examiner argued that the claim language reciting that the "composition comprises an antisense oligonucleode of SEQ ID NO: 1" embraces any variants or fragments of antisense oligonucleotides having SEQ ID NO: 1 and reads broadly on different species of antisense oligonucleotides having SEQ ID NO: 1.

Without acquiescing in the rejection, Applicants have amended claim 1 to recite that the composition "comprises the antisense oligonucleotide of SEQ ID NO: 1" as suggested by the Examiner. Support for the amendment is also found throughout the application as filed; exemplary support can be found, for example, in Paragraphs [0054], [0055], [0089], and Example 17 of the specification as published. Applicants respectfully submit that Claims 1-3 and 7-8 as amended are in compliance with the written description requirement and request withdrawal of the rejection.

Claim Rejections Under 35 U.S.C. §112, Enablement

The Examiner maintained the rejection of Claims 1-3 and 7-8 as allegedly failing to comply with the enablement requirement. The Examiner again argued that the claim language reciting that the "composition comprises an antisense oligonucleotide of SEQ ID NO: 1" embraces any variants or fragments of antisense oligonucleotides having SEQ ID NO: 1 and reads broadly on different species of antisense oligonucleotides having SEQ ID NO: 1.

As discussed above, Applicants have amended claim 1 to recite that the composition "comprises the antisense oligonucleotide of SEQ ID NO: 1", which the Examiner had indicated

would be remedial. Applicants respectfully submit that the Claims 1-3 and 7-8 as amended are in compliance with the enablement requirement and request the withdrawal of the rejection.

Double Patenting Rejection over U.S. Patent 6,169,079

Claims 1-3 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable in view of Claims 2-3 of U.S. Patent No. 6,169,079 ("the '079 patent"). The Examiner asserted that the claims are patentably indistinct from the reference claims of the '079 patent because the scope Claims 2-3 of the '079 patent embraces the patent protection sought by the scope of the instant claims. However, the Examiner's rationale is improper. Whether or not the scope of Claims 1-3 of the instant application is dominated by the scope of Claims 2-3 of the '079 patent is not dispositive. Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or non-statutory double patenting grounds, cannot support a double patenting rejection. *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986).

In determining whether a non-statutory basis exists for a double patenting rejection, the first analysis is whether any claim in the application defines an invention that is merely an obvious variation of an invention claimed in the patent. Such analysis parallels the guidelines for analysis of a 35 U.S.C. §103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991).

In the present situation, the '079 patent claims a "method of inhibiting the synthesis of human intercellular adhesion molecule-1 in a cell or tissue" or "a method of treating a human having a disease with an inflammatory component which is modulated by changes in human intercellular adhesion molecule-1". The methods comprise contacting the cell or tissue (reference Claim 2) or a human (reference Claim 3) with *any* antisense oligonucleotide targeted to "a transcription initiation site, a translation initiation site, a 5'-untranslated sequence, a coding region or a 3'-untranslated sequence of an mRNA encoding human intercellular adhesion molecule-1". Accordingly, Claims 2-3 cover the use of an infinite number of antisense

molecules to generically "inhibit synthesis" of ICAM-1, or to generically treat "a human having a disease with an inflammatory component".

In contrast to the generic claims, the instant claims are directed to a method of treating a species of disease, pouchitis, with a composition that includes an antisense oligonucleotide having the sequence of SEQ ID NO: 1. The instant claims are not obvious variants of generic Claims 2-3 from the '079 patent because they recite a particular use (treatment of pouchitis) using a particular compound, SEQ ID NO: 1. The Examiner provides no evidence of why the species claimed in the instant application would be obvious in view of the generic claims from the '079 patent. For these reasons, a rejection for obviousness type double patenting is improper and Applicants respectfully request the withdrawal of this rejection.

Double Patenting Rejections over U.S. Patent 5,591,623

Claim 1 was also rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over Claims 2 and 4 of U.S. Patent No. 5,591,623 ("the '623 patent") in view of Patel et al. (1995, *European Journal of Gastroenterology & Hepatology* 7:1037-1041). The Examiner argued that the claims are not patentably distinct from each other because SEQ ID NO: 1 of the instant claims is identical to SEQ ID NO: 22 of the reference claims of the '623 patent.

The reference claims of the '623 patent recite a "method of inhibiting synthesis of intercellular adhesion molecules in a cell comprising contacting the cell in vitro" with "an oligonucleotide having SEQ ID NO: 22" (Claim 2) or with "an oligonucleotide having SEQ ID NO: 1, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 20, 21, 23, 24, 25, 26 or 27" (Claim 4). The Examiner has argued that although the conflicting claims are not identical, they are not patentably distinct from each other because SEQ ID NO: 1 of the instant claims is identical to SEQ ID NO: 22 of the reference claims. Furthermore, the Examiner asserted that while the reference claims do not expressly recite a "method of treating pouchitis in a human in need thereof", the methods of the reference claims embrace the instantly claimed invention because the specification of the '623 patent discloses that "an animal suspected of having a disease which can be treated by decreasing the expression of ICAM-1" is "treated by administering oligonucleotides in accordance with this invention". The Examiner cited Patel et al., which teaches a correlation between high plasma level of ICAM-1 and pouchitis.

Applicants respectfully submit that the double patenting issue is predicated on whether the conflicting claims are patentably distinct from one another, rather than what the patent discloses. A double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the non-obviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967) (emphasis added). While the specification of the '623 patent provides the disclosure as recited above, the cited claims of the '623 patent relate to methods of inhibiting synthesis of intercellular adhesion molecules in a cell ***in vitro***. In contrast, instant Claim 1 is directed towards an ***in vivo*** method of treating a specific disease, pouchitis in a human, with a pharmaceutical composition that comprises the antisense oligonucleotide of SEQ ID NO: 1. The instant claims recite a new use, the *in vivo* treatment of pouchitis in a human, as well as a distinct element, the pharmaceutical composition.

Furthermore, although Patel discloses a correlation between high plasma level of ICAM-1 and pouchitis, there is no teaching in Patel that decreasing ICAM-1 levels would treat pouchitis. Patel suggests the use of ICAM-1 as a *marker* of continuing inflammation, but does not suggest that inhibiting this marker would provide a therapeutic benefit for pouchitis. Accordingly, Patel does not demonstrate that the *in vivo* claims in the instant application relating to pouchitis are obvious variants of the *in vitro* claims from the '623 patent.

Therefore, in view of the foregoing remarks, Applicants submit that the method of treating pouchitis *in vivo* of the instant application is not an obvious variant of the *in vitro* methods recited in Claims 2 and 4 of the '623 patent. Applicants therefore respectfully request the withdrawal of this rejection.

Conclusion

Applicants submit that the present application is in condition for allowance and respectfully requests an action to that effect. If any issues remain, the Examiner is invited to contact Applicants' counsel at the number provided below in order to resolve such issues promptly.

Respectfully submitted,

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